

5/05/05

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSSPTA1612RXD

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * * Welcome to STN International * * * * * * * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 10 MAR 22 KOREPAT now updated monthly; patent information enhanced
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 12 MAR 22 PATDPASPC - New patent database available
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 14 APR 04 EPFULL enhanced with additional patent information and new fields
NEWS 15 APR 04 EMBASE - Database reloaded and enhanced
NEWS 16 APR 18 New CAS Information Use Policies available online
NEWS 17 APR 25 Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAPLUS and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS 18 APR 28 Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAPLUS

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

| | |
|------------|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS INTER | General Internet Information |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS PHONE | Direct Dial and Telecommunication Network Access to STN |
| NEWS WWW | CAS World Wide Web Site (general information) |

Enter NEWS followed by the item number or name to see news on that specific topic.

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result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 14:28:23 ON 05 MAY 2005

=> file registry
COST IN U.S. DOLLARS

| | |
|-----------------------------|--------------------------|
| SINCE FILE
ENTRY
0.21 | TOTAL
SESSION
0.21 |
|-----------------------------|--------------------------|

FILE 'REGISTRY' ENTERED AT 14:28:30 ON 05 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 MAY 2005 HIGHEST RN 849790-35-8
DICTIONARY FILE UPDATES: 4 MAY 2005 HIGHEST RN 849790-35-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

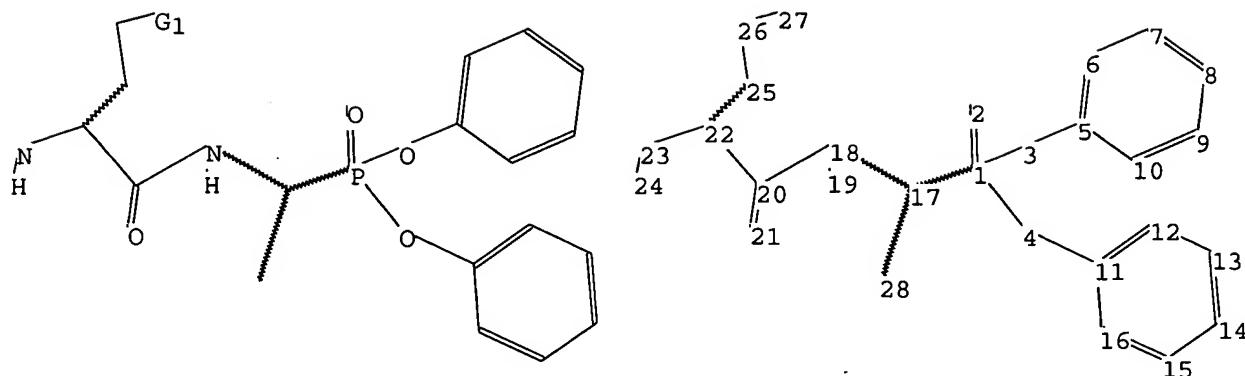
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Crossover limits have been increased. See **HELP CROSSOVER** for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

```
=>  
Uploading C:\Program Files\Stnexp\Queries\10774562.str
```

5/05/05



chain nodes :
1 2 3 4 17 18 19 20 21 22 23 24 25 26 27 28
ring nodes :
5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
1-2 1-3 1-4 1-17 3-5 4-11 17-18 17-28 18-19 18-20 20-21 20-22 22-23
22-25 23-24 25-26 26-27
ring bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16
exact/norm bonds :
1-2 1-3 1-4 3-5 4-11 17-18 18-20 20-21 22-23 26-27
exact bonds :
1-17 17-28 18-19 20-22 22-25 23-24 25-26
normalized bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16

G1:C,O,S,N

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS

L1 STRUCTURE UPLOADED

=> d 11
L1 HAS NO ANSWERS
L1 STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s11
SL1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.

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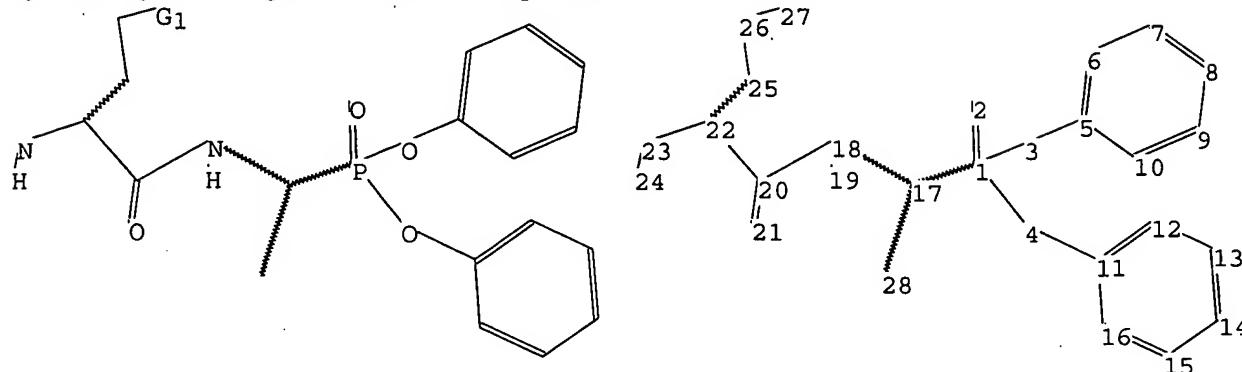
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s 11 ful
FULL SEARCH INITIATED 14:29:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10774562.str



chain nodes :

1 2 3 4 17 18 19 20 21 22 23 24 25 26 27 28

ring nodes :

5 6 7 8 9 10 11 12 13 14 15 16

chain bonds :

1-2 1-3 1-4 1-17 3-5 4-11 17-18 17-28 18-19 18-20 20-21 20-22 22-23
22-25 23-24 25-26 26-27

ring bonds :

5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16

exact/norm bonds :

1-2 1-3 1-4 3-5 4-11 17-18 18-20 20-21 22-23 26-27

exact bonds :

1-17 17-28 18-19 20-22 22-25 23-24 25-26

normalized bonds :

5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16

G1:C,O,S,N

Match level :

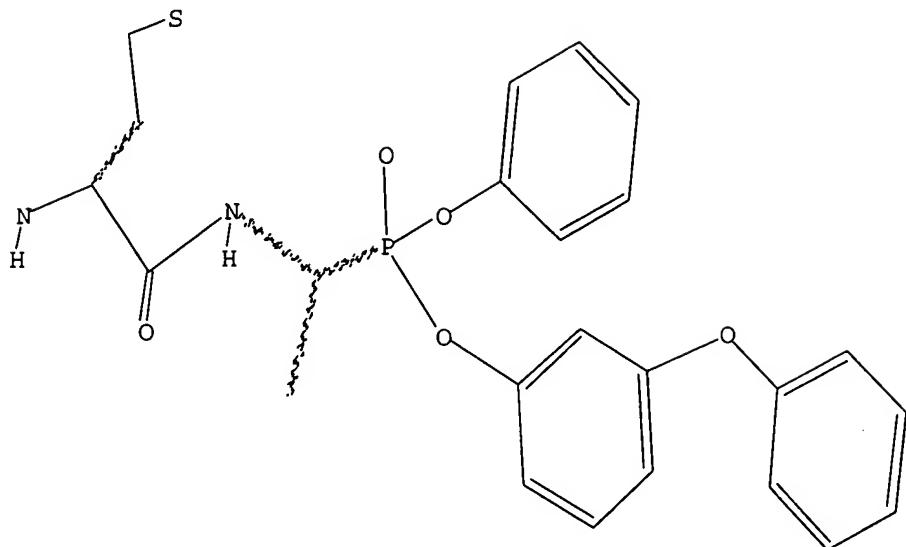
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS

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L3 STRUCTURE UPLOADED

=> d 13
L3 HAS NO ANSWERS
L3 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 13
SAMPLE SEARCH INITIATED 14:31:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 0 TO 0
PROJECTED ANSWERS: 0 TO 0

L4 0 SEA SSS SAM L3

=> s 13 ful
FULL SEARCH INITIATED 14:31:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1 TO ITERATE

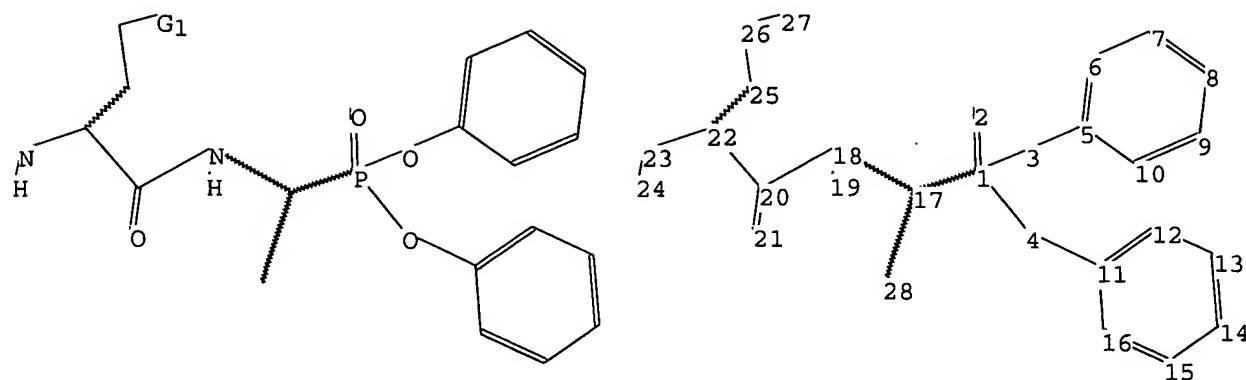
100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L5 0 SEA SSS FUL L3

=>
Uploading C:\Program Files\Stnexp\Queries\10774562.str

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chain nodes :
1 2 3 4 17 18 19 20 21 22 23 24 25 26 27 28
ring nodes :
5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
1-2 1-3 1-4 1-17 3-5 4-11 17-18 17-28 18-19 18-20 20-21 20-22 22-23
22-25 23-24 25-26 26-27
ring bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16
exact/norm bonds :
1-2 1-3 1-4 3-5 4-11 17-18 18-20 20-21 22-23 26-27
exact bonds :
1-17 17-28 18-19 20-22 22-25 23-24 25-26
normalized bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16

G1:C,O,S,N

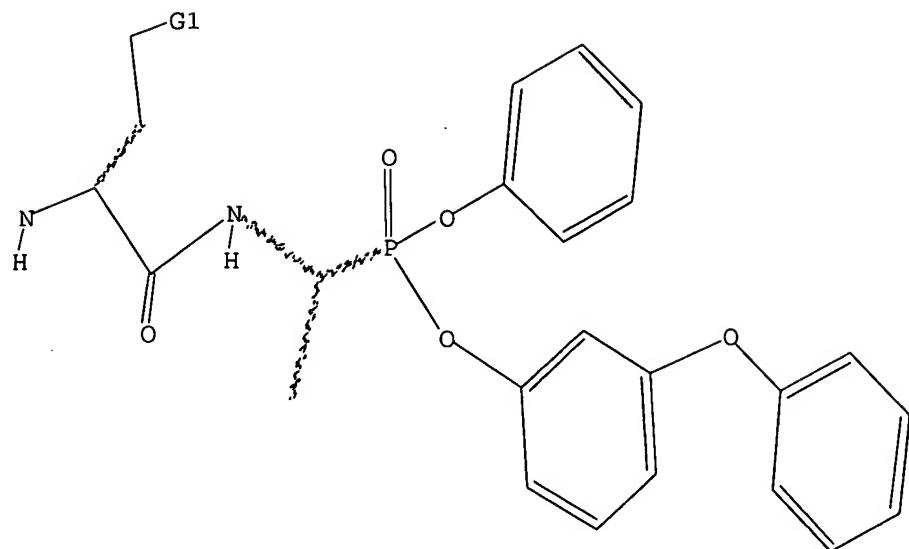
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS

L6 STRUCTURE UPLOADED

=> d 16
L6 HAS NO ANSWERS
L6 STR

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G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

```
=> s 16
SAMPLE SEARCH INITIATED 14:32:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE
```

```
100.0% PROCESSED      0 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01
```

```
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                           BATCH   **COMPLETE**
PROJECTED ITERATIONS:      0 TO      0
PROJECTED ANSWERS:         0 TO      0
```

L7 0 SEA SSS SAM L6

```
=> s 16 ful
FULL SEARCH INITIATED 14:33:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      1 TO ITERATE
```

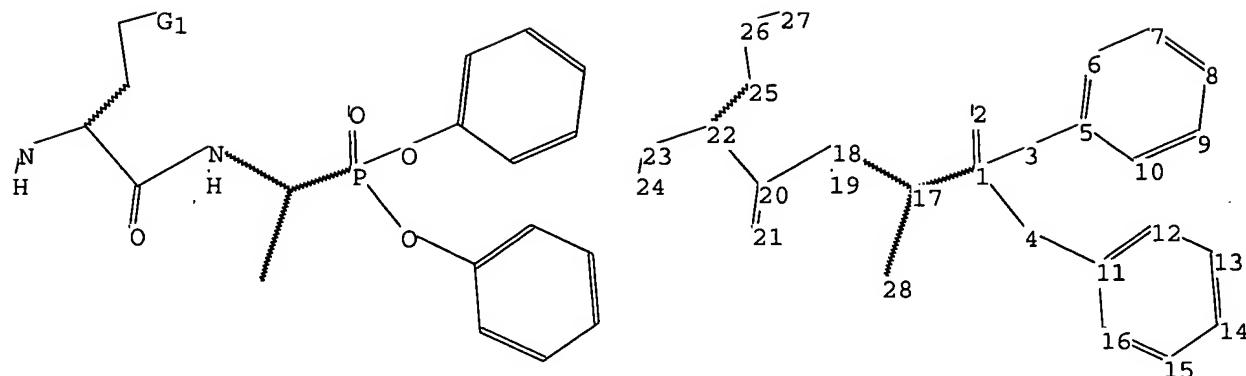
```
100.0% PROCESSED      1 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01
```

L8 0 SEA SSS FUL L6

```
=>
Uploading C:\Program Files\Stnexp\Queries\10774562.str
```

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chain nodes :
1 2 3 4 17 18 19 20 21 22 23 24 25 26 27 28
ring nodes :
5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
1-2 1-3 1-4 1-17 3-5 4-11 17-18 17-28 18-19 18-20 20-21 20-22 22-23
22-25 23-24 25-26 26-27
ring bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16
exact/norm bonds :
1-2 1-3 1-4 3-5 4-11 17-18 18-20 20-21 22-23 26-27
exact bonds :
1-17 17-28 18-19 20-22 22-25 23-24 25-26
normalized bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16

G1:C,O,S,N

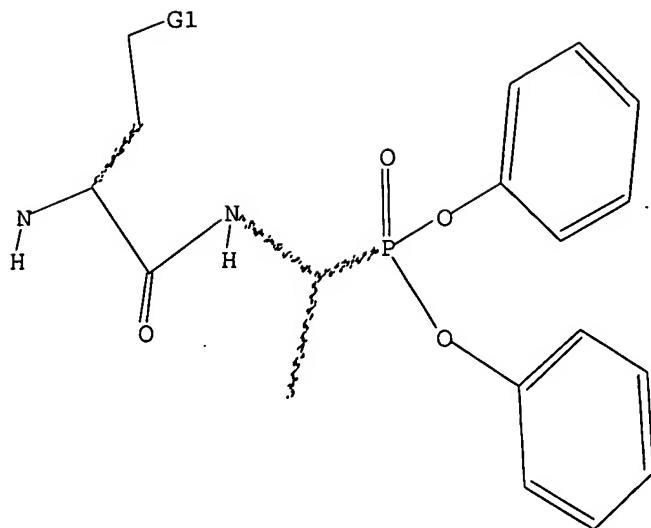
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS

L9 STRUCTURE UPLOADED

=> d 19
L9 HAS NO ANSWERS
L9 STR

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G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s 19

SAMPLE SEARCH INITIATED 14:34:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 24 TO ITERATE

100.0% PROCESSED 24 ITERATIONS
SEARCH TIME: 00.00.01

5 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 187 TO 773
PROJECTED ANSWERS: 5 TO 234

L10 5 SEA SSS SAM L9

=> s 19 ful

FULL SEARCH INITIATED 14:34:19 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 476 TO ITERATE

100.0% PROCESSED 476 ITERATIONS
SEARCH TIME: 00.00.01

78 ANSWERS

L11 78 SEA SSS FUL L9

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 647.90 | 648.11 |

FILE 'CAPLUS' ENTERED AT 14:34:23 ON 05 MAY 2005
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FILE COVERS 1907 - 5 May 2005 VOL 142 ISS 19
FILE LAST UPDATED: 4 May 2005 (20050504/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l11
L12          17 L11

=> d abs bib hitstr 1-17
```

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L12 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AB This invention provides compds. and methods for using them to inhibit the growth of a microorganism that expresses peptide deformylase. Drugs such as nitroimycin, bleomycin, ciprofloxacin, can be bound to linkers.

AN 2004430717 CAPLUS

DN 140:423025

TI Peptide deformylase activated prodrugs

IN Ballatore, Carlo; Doppalapudi, Venkata Ramana; Sergeeva, Maria V.

PA Newbiotics, Inc., USA

SO PCT Int. Appl., 41 pp.

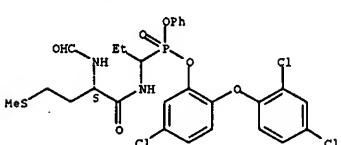
CODEN: PIXXD2

DT Patent
LA English

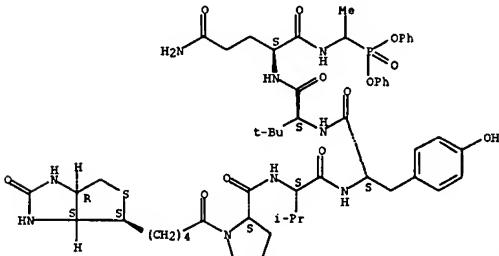
FAN,CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2004043400 | A2 | 20040527 | WO 2003-US36124 | 20031114 |
| WO 2004043400 | A3 | 20040930 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GR, HU, IL, IS, JP, KR, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TH, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GR, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, MU, TZ, IM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004236096 | A1 | 20041125 | US 2003-714255 | 20031114 |
| PRAI US 2002-42671P | P | 20021114 | | |
| OS MARPAT 140:429025 | | | | |
| IT 691883-26-8P | | | | |
| RL: SPI (Synthetic preparation); THU (Therapeutic use); BIOL (Biological Study); PRP (Preparation); USES (Uses); (peptide deformylase activated prodrugs) | | | | |
| RN 691883-26-8 CAPLUS | | | | |
| CN Phosphonic acid, [1-[(2S)-2-(formylamino)-4-(methylthio)-1-oxobutylamino]propyl]-, 5-chloro-2-(2,4-dichlorophenoxy)phenyl phenyl ester (9CI) (CA INDEX NAME) | | | | |

Absolute stereochemistry.



L12 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AB Structurally diverse organophosphonate inhibitors targeting the active site of the enzyme were used to investigate the relationship of the active site and the dimer interface of wild-type protease in solution. Positional scanning synthetic combinatorial libraries revealed Kaposi's sarcoma-associated herpesvirus protease to be highly specific, even at sites distal to the peptide bond undergoing hydrolysis. Specificity results were used to synthesize a hexapeptide diphenylphosphonate inhibitor of Kaposi's sarcoma-associated herpesvirus protease. The transition state analog inhibitors covalently phosphorylate the active site serine freezing the enzyme structure during catalysis. An NMR-based assay was developed to monitor the native monomer-dimer equilibrium in solution and was used

to demonstrate the effect of protease inhibition on the quaternary structure of the enzyme. NMR, CD, and size exclusion chromatog. anal. showed that active site inhibition strongly regulates the binding affinity of the monomer-dimer equilibrium at the spatially sep. dimer interface of the protease, shifting the equilibrium to the dimeric form of the enzyme. Furthermore, inhibitor studies revealed that the catalytic cycles of the spatially sep. active sites are independent. These results (i) provide direct evidence that peptide bond hydrolysis is integrally linked to the quaternary structure of the enzyme, (ii) establish a mol. mechanism of protease activation and stabilization during catalysis, and (iii) highlight potential implications of substoichiometric inhibition of the viral protease in developing herpesviral therapeutics.

AN 2004:413887 CAPLUS

DN 141:161603

TI Communication between the active sites and dimer interface of a herpesvirus protease revealed by a transition-state inhibitor

AU Marnett, Alan B.; Nomura, Anson M.; Shima, Nobuhisa; De Montellano, Paul R. Ortiz; Craik, Charles S.

CS Program in Chemistry and Chemical Biology, Department of Pharmaceutical Chemistry, University of California, San Francisco, CA, 94143, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2004), 101(18), 6870-6875

CODEN: PNASAA; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

IT 727423-06-5

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(communication between active sites and dimer interface of herpesvirus protease revealed by transition-state inhibitor)

RN 727423-06-5 CAPLUS

CN L-Glutamamide, 1-[5-[(3S,4S,6S)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-1-prolyl-L-valyl-L-tyrosyl-3-methyl-L-valyl-N-[1-(diphenyloxyphosphoryl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AB Granzyme M is a member of a family of granule serine proteases that participate in target cell death initiated by cytotoxic lymphocytes. The enzyme is almost exclusively expressed in NK cell types. Granzyme M cleaves at the carbonyl side of amino acids with long, hydrophobic side chains like Met, Leu, and Nle. To further study the substrate specificity of the enzyme, a series of peptide thiobenzyl esters was synthesized. The hydrolysis of the substrates with murine and human recombinant forms of granzyme M was observed. The results show that the enzyme has a strong preference for Pro at the P2 position and Ala, Ser, or Asp at the P3 position. These results suggest that the protein residues of the S2 and S3 subsites form important binding interactions that aid in the selection of specific natural substrates for granzyme M. A series of inhibitors was also tested with granzyme M. None of the inhibitors were effective inactivators of granzyme M, including the general serine protease inhibitor, 3,4-dichloroisocoumarin, which is usually a potent inactivator of serine proteases. This suggests that inhibition of granzyme M may be difficult. Also reported for the first time is the method utilized to isolate granzyme M used in this and previous publications. The observations in this paper will be valuable in development of new potent inhibitors for granzyme M as well as assist in determining the biol. function of the enzyme.

AN 2004:30246 CAPLUS

DN 140:402221

TI Subsite specificities of granzyme M: a study of inhibitors and newly synthesized thiobenzyl ester substrates

AU Rukamp, Brian J.; Kam, Chih-Min; Natarajan, Sudha; Bolton, Brad W.; Smyth, Mark J.; Kelly, Janice M.; Powers, James C.

CS The School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332-0400, USA

SO Archives of Biochemistry and Biophysics (2004), 422(1), 9-22

CODEN: ABBIA4; ISSN: 0003-9861

PB Elsevier Science

DT Journal

LA English

IT 688789-07-3 688789-08-4 688789-09-5

688789-10-8 688789-11-9

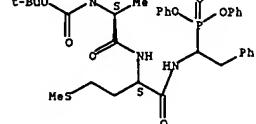
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(subsite specificities of granzyme M for inhibitors and newly synthesized thiobenzyl ester substrates)

RN 688789-07-3 CAPLUS

CN L-Methionamide, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-N-[(diphenyloxyphosphoryl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

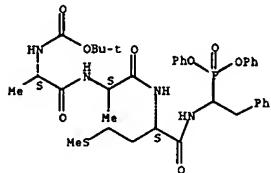


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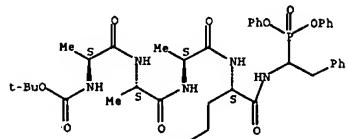
L12 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 RN 688789-08-4 CAPLUS
 CN L-Methioninamide, N-[{(1,1-dimethylethoxy)carbonyl}-L-alanyl-L-alanyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 688789-09-5 CAPLUS
 CN L-Methioninamide, N-[{(1,1-dimethylethoxy)carbonyl}-L-alanyl-L-alanyl-L-alanyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

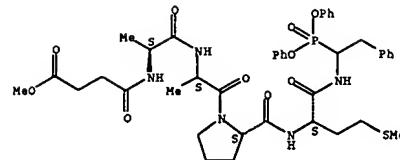
Absolute stereochemistry.



RN 688789-10-8 CAPLUS
 CN L-Methioninamide, N-[{(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-L-prolyl}-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

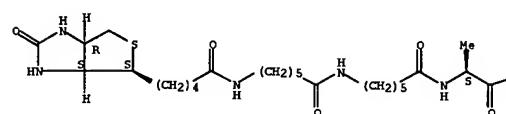
L12 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



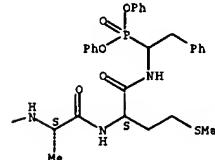
RN 688789-11-9 CAPLUS
 CN L-Methioninamide, N-[{6-[(6-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino}-1-oxohexyl]-L-alanyl-L-alanyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD

L12 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AB In this paper, the authors present a parallel synthesis of several series of dipeptide di-Ph phosphonates that are known to be irreversible inhibitors of serine proteases. Polymer-assisted solution-phase synthesis (PASP) is used for the rapid and clean coupling between various α -aminoalkyl di-Ph phosphonate ester building blocks and compon. available or easily accessible amino acids. These compds. were used for the rapid profiling of dipeptidyl peptidase II (DPP II) and the closely related dipeptidyl peptidase IV (DPP IV). A highly selective DPP II inhibitor was identified, N-cyclopentylglycyl-NHCH₂(Ph)P(O)Ph₂, that will be useful to discriminate between DPP II and DPP IV in biol. systems in order to further elucidate the biol. function of DPP II.

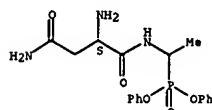
AN 2003;89910 CAPLUS
 DN 138:287948
 TI Rapid Parallel Synthesis of Dipeptidyl Diphenyl Phosphonate Esters as Inhibitors of Dipeptidyl Peptidases
 AU Senten, Kristel; Danieels, Liebeth; Van der Veken, Pieters; De Meester, Ingrid; Lambrechts, Anne-Marie; Scharpe, Simon; Haemers, Achiel; Augustyns, Koen
 CS Department of Medicinal Chemistry, University of Antwerp, Antwerp, B-2610, Belg.
 SO Journal of Combinatorial Chemistry (2003), 5(3), 336-344
 CODEN: JCCHPF ISSN: 1520-4766
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 138:287948
 IT 503820-02-8P 503820-04-0P 503820-16-4P
 503820-18-6P 503820-20-0P 503820-32-4P
 503820-36-8P 503820-38-0P 503820-40-4P
 503820-42-6P 503820-44-8P 503820-46-0P
 503820-58-4P
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and biol. activity of dipeptide di-Ph phosphonate esters as inhibitors of dipeptidyl peptidases)

RN 503820-02-8 CAPLUS
 CN Phosphonic acid, [1-[(2S)-2,4-diamino-1,4-dioxobutyl]amino]ethyl]-, diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CH 1

CRN 503820-01-7
 CMF C18 H22 N3 O5 P

Absolute stereochemistry.



CH 2

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L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CRN 76-05-1
CHF C2 H F3 O2

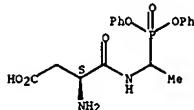


RN 503820-04-0 CAPLUS
CN Butanoic acid, 3-amino-4-[(1-(diphenoxypheophenyl)ethyl)amino]-4-oxo-,
(3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 503820-03-9
CNF C18 H21 N2 O6 P

Absolute stereochemistry.



CM 2

CRN 76-05-1
CNF C2 H F3 O2

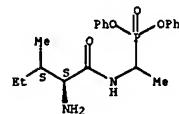


RN 503820-16-4 CAPLUS
CN Phosphonic acid, [1-[(25,3S)-2-amino-3-methyl-1-oxopentyl]amino]ethyl-,
diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 503820-15-3
CNF C20 H27 N2 O4 P

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Absolute stereochemistry.



CM 2

CRN 76-05-1
CNF C2 H F3 O2

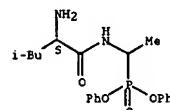


RN 503820-18-6 CAPLUS
CN Phosphonic acid, [1-[(2S)-2-amino-4-methyl-1-oxopentyl]amino]ethyl-,
diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 503820-17-5
CNF C20 H27 N2 O4 P

Absolute stereochemistry.



CM 2

CRN 76-05-1
CNF C2 H F3 O2

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

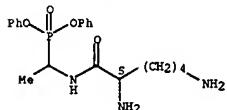


RN 503820-20-0 CAPLUS
CN Phosphonic acid, [1-[(25)-2,6-diamino-1-oxohexyl]amino]ethyl-, diphenyl
ester, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 503820-19-7
CNF C20 H28 N3 O4 P

Absolute stereochemistry.



CM 2

CRN 76-05-1
CNF C2 H F3 O2



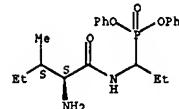
RN 503820-32-4 CAPLUS
CN Phosphonic acid, [1-[(25,3S)-2-amino-3-methyl-1-oxopentyl]amino]propyl-,
diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 503820-31-3
CNF C21 H29 N2 O4 P

Absolute stereochemistry.

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CM 2

CRN 76-05-1
CNF C2 H F3 O2

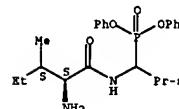


RN 503820-36-8 CAPLUS
CN Phosphonic acid, [1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]butyl-,
diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 503820-35-7
CNF C22 H31 N2 O4 P

Absolute stereochemistry.



CM 2

CRN 76-05-1
CNF C2 H F3 O2



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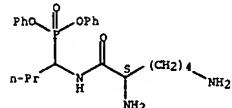
5/05/05

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 RN 503820-38-0 CAPLUS
 CN Phosphonic acid, [1-[(2S)-2,6-diamino-1-oxohexyl]amino]butyl-, diphenyl ester, trifluoroacetate (9CI) (CA INDEX NAME)

CH 1

CRN 503820-37-9
 CMF C22 H32 N3 O4 P

Absolute stereochemistry.



CH 2

CRN 76-05-1
 CMF C2 H F3 O2



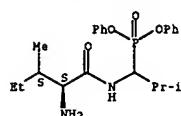
RN 503820-40-4 CAPLUS
 CN Phosphonic acid, [1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-2-methylpropyl-, diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CH 1

CRN 503820-39-1
 CMF C22 H31 N2 O4 P

Absolute stereochemistry.

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CH 2

CRN 76-05-1
 CMF C2 H F3 O2

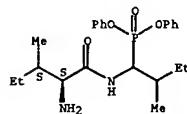


RN 503820-42-6 CAPLUS
 CN Phosphonic acid, [1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-2-methylbutyl-, diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CH 1

CRN 503820-41-5
 CMF C23 H33 N2 O4 P

Absolute stereochemistry.



CH 2

CRN 76-05-1
 CMF C2 H F3 O2

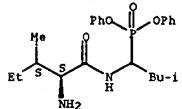
L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 503820-44-8 CAPLUS
 CN Phosphonic acid, [1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-3-methylbutyl-, diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CH 1

CRN 503820-43-7
 CMF C23 H33 N2 O4 P

Absolute stereochemistry.



CH 2

CRN 76-05-1
 CMF C2 H F3 O2



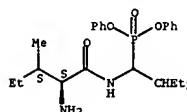
RN 503820-46-0 CAPLUS
 CN Phosphonic acid, [1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-2-ethylbutyl-, diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CH 1

CRN 503820-45-9
 CMF C24 H35 N2 O4 P

Absolute stereochemistry.

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CH 2

CRN 76-05-1
 CMF C2 H F3 O2

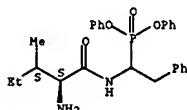


RN 503820-58-4 CAPLUS
 CN Phosphonic acid, [1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-2-phenylethyl-, diphenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CH 1

CRN 503820-57-3
 CMF C26 H31 N2 O4 P

Absolute stereochemistry.



CH 2

CRN 76-05-1
 CMF C2 H F3 O2

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L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



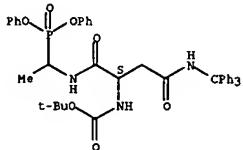
IT 503821-05-4P 503821-06-5P 503821-12-3P
503821-13-4P 503821-14-5P 503821-21-4P
503821-23-6P 503821-24-7P 503821-25-8P
503821-26-9P 503821-27-0P 503821-28-1P
503821-35-0P

RL RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); preparation and biol. activity of dipeptide di-Ph phosphonate esters as inhibitors of dipeptidyl peptidases

RN 503821-05-4 CAPLUS

CN Carbamic acid, [(1S)-1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-oxo-3-[(triphenylmethyl)amino]propyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

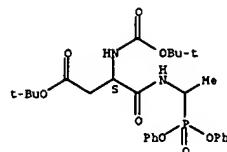


RN 503821-06-5 CAPLUS

CN Butanoic acid, 3-[(1,1-dimethylethoxy)carbonyl]amino)-4-[(1-(diphenoxypyrophosphinyl)ethyl)amino]-4-oxo-, 1,1-dimethylethyl ester, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

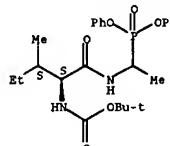
L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 503821-12-3 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

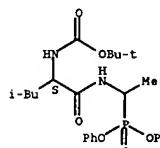
Absolute stereochemistry.



RN 503821-13-4 CAPLUS

CN Carbamic acid, [(1S)-1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

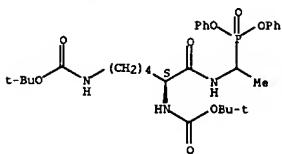


RN 503821-14-5 CAPLUS

CN Carbamic acid, [(1S)-1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-1,5-pentanediyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

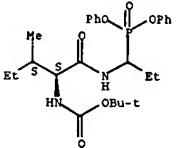
Absolute stereochemistry.



RN 503821-21-4 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1-(diphenoxypyrophosphinyl)propyl)amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

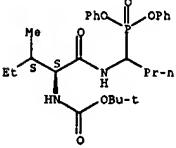
Absolute stereochemistry.



RN 503821-23-6 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1-(diphenoxypyrophosphinyl)butyl)amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



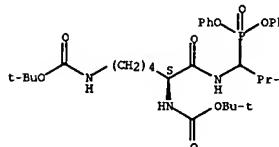
RN 503821-24-7 CAPLUS

CN Carbamic acid, [(1S)-1-[(1-(diphenoxypyrophosphinyl)butyl)amino]carbonyl]-1,5-pentanediyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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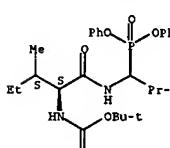
L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 503821-25-8 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1-(diphenoxypyrophosphinyl)-2-methylpropyl)amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

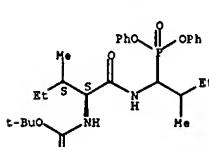
Absolute stereochemistry.



RN 503821-26-9 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1-(diphenoxypyrophosphinyl)-2-methylbutyl)amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

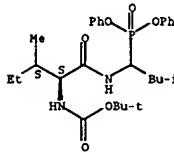


RN 503821-27-0 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1-(diphenoxypyrophosphinyl)-3-methylbutyl)amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

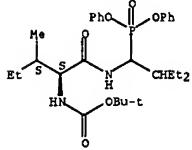
5/05/05

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Absolute stereochemistry.



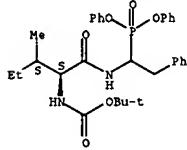
RN 503821-28-1 CAPLUS
CN Carbamic acid, [(1S,2S)-1-{{[1-(diphenoxypyrophosphinyl)-2-ethylbutyl]amino}carbonyl}-2-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 503821-35-0 CAPLUS
CN Carbamic acid, [(1S,2S)-1-{{[1-(diphenoxypyrophosphinyl)-2-phenylethyl]amino}carbonyl}-2-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AB The aim of the invention is to develop a method for producing catalytic antibodies to proteins and peptides, in particular to gp120, using animals with spontaneous or induced autoimmune pathologies. Various methods for producing catalytic antibodies are disclosed. The inventive methods make it possible to create a catalytic vaccine which, when injected to a patient exhibits adhesive properties in relation to specific antigen simultaneously with antigen-degrading function, thereby inhibiting the progression of the disease. Said invention discloses the method for the autoimmunization of SJL mice by fusion proteins containing a classical peptide epitope (for example, myelin basic protein or fragments thereof) and the potential substrate of the target catalytic antibody (for example, HIV-1 gp120 or fragments thereof). The invention also comprises the method for immunizing autoimmune animals with highly reactive chemical compds., which can select catalytic clones containing peptide fragments of proteolytically degraded gp120.

AN 2002832912 CAPLUS
DN 137:351494
TI Method for producing catalytic antibodies, antigens for immunization and nucleotide sequences
IN Gabibov, Alexandr Gabibovich; Kolesnikov, Aleksandr Vladimirovich; Ponomarenko, Natalya Alexandrovna; Aleksandrovna, Elena Sergeevna; Borobiev, Ivan Ivanovich; Demin, Alexander Viktorovich
PA ASGL - Farmatsevticheskie Innovatsii, Zakrytoe Aktionernoe Obshchestvo, Russia
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA Russian
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| PI WO 2002086058 | A2 | 20021031 | WO 2002-RU177 | 20020418 |
| WO 2002086058 | C2 | 20021212 | | |
| WO 2002086058 | A3 | 20030123 | | |
| W: AU, BG, BY, CA, CN, CZ, EE, HU, IL, JP, KR, NO, PL, SK, UA, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR | | | | |
| RU 2221873 | C2 | 20040120 | RU 2001-110759 | 20010424 |
| EP 1394261 | A2 | 20040303 | EP 2002-739002 | 20020418 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI, CY, TR | | | | |
| JP 2004527248 | T2 | 20040909 | JP 2002-583573 | 20020418 |
| US 2004265975 | A1 | 20041230 | US 2004-475706 | 20040512 |
| PRAI RU 2001-110759 | A | 20010424 | | |
| WO 2002-RU177 | W | 20020418 | | |

IT 473464-36-7P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(polyclonal catalytic antibodies preparation, antigens for immunization,

and nucleotide sequences using animals with spontaneous or induced autoimmune pathologies)

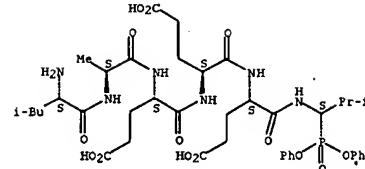
RN 473464-36-7 CAPLUS
CN L-a-Glutamine, L-leucyl-L-alanyl-L-a-glutamyl-L-a-glutamyl-N-[(1S)-1-(diphenoxypyrophosphinyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10714255

L12 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



5/05/05

L12 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AB This letter describes the parallel synthesis of dipeptide p-nitroanilides and dipeptides di-Ph phosphonates, compds. that can be used as substrates and irreversible inhibitors for the rapid profiling of dipeptidyl peptidases. A polymer-assisted solution-phase synthesis was used for a rapid

and clean coupling between easily available building blocks.

AN 2001:905514 CAPLUS

DN 136:247867

TI Polymer-assisted solution-phase parallel synthesis of dipeptide p-nitroanilides and dipeptide diphenyl phosphonates

AU Sentein, Kristel; Van der Veken, Pieter; Bal, Gunther; Haemers, Achiel; Augustyns, Koen

CS Department of Medicinal Chemistry, University of Antwerp (UIA), Antwerp, B-2610, Belg.

SO Tetrahedron Letters (2001), 42(52), 9135-9138

CODEN: TELELV, ISSN: 0040-4039

PP Elsevier Science Ltd.

DT JUN

LA English

CASREACT 136:247867

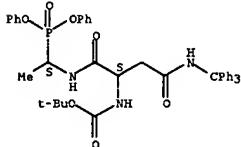
IT 404012-65-3P 404012-66-4P 404012-69-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); (solution-phase parallel synthesis of dipeptide p-nitroanilides and dipeptide di-Ph phosphonates)

RN 404012-65-3 CAPLUS

CN Carbamic acid, [(1S)-1-[(1S)-1-(diphenoxypyrophosphinyl)ethyl]amino]carbonyl]-3-oxo-3-[(triphenylmethyl)amino]propyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



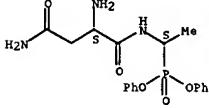
RN 404012-66-4 CAPLUS

CN Butanoic acid, 3-[(1,1-dimethylethoxy)carbonyl]amino]-4-[(1S)-1-(diphenoxypyrophosphinyl)ethyl]amino]-4-oxo-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

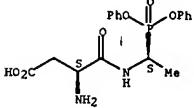
Absolute stereochemistry.



RN 404012-76-6 CAPLUS

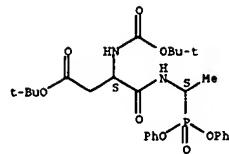
CN Butanoic acid, 3-amino-4-[(1S)-1-(diphenoxypyrophosphinyl)ethyl]amino]-4-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

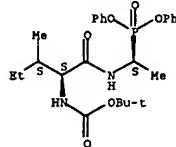
L12 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 404012-69-7 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[(1S)-1-(diphenoxypyrophosphinyl)ethyl]amino]carbonyl]-2-methylbutyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



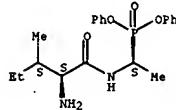
IT 178150-13-5P 404012-75-5P 404012-76-6P

RL: SPN (Synthetic preparation); PREP (Preparation); (solution-phase parallel synthesis of dipeptide p-nitroanilides and dipeptide di-Ph phosphonates)

RN 178150-13-5 CAPLUS

CN Phosphonic acid, [(1S)-1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]ethyl-, diphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

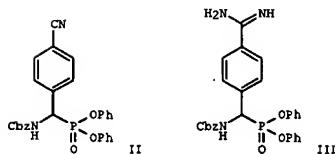
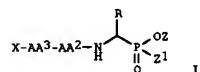


RN 404012-75-5 CAPLUS

CN Phosphonic acid, [(1S)-1-[(2S)-2,4-diamino-1,4-dioxobutyl]amino]ethyl-,

L12 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L12 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN GI



AB Peptidyl α -aminoalkylphosphonic acid diesters with basic substituents I ($R = Ph, CH_2Ph, C1-6$ alkyl substituted with amidino, guanidino, isothioureido, or amino; $Z = C1-6$ perfluoroalkyl, Ph, Ph substituted with J ; $Z1 = C1-6$ alkoxy, halor; $J = halo, Cl-6$ alkyl, $C1-6$ perfluoroalkyl, $C1-6$ alkoxy, N_2O_2 , CN, OH, CO_2H , amino, $C1-6$ alkylamino, $C2-12$ dialkylamino, $C1-6$ acyl, $C1-6$ alkoxy carbonyl, $C1-6$ alkylthio; AA_2 , AA_3 = independently bond, or unblocked D-, L-, or achiral amino acid residue; $X = Y-CO, Y-SO_2$; $Y = Ph-CH=CH, (2-furyl)CH=CH, (2-thienyl)CH=CH, (2-Pyridyl)CH=CH, 2\text{-phenoxypyphenyl}, 3\text{-phenoxypyphenyl},$ substituted Ph, $C1-6$ alkenyl substituted with a heterocyclic group, (un)substituted Ph, or (un)substituted naphthyl) and pharmaceutically acceptable salts thereof were prepared as compds. for use in inhibiting serine proteases with trypsin-like specificity and as anti-inflammatory agents, anticoagulants, and anti-tumor agents. Thus, condensation of 9.75 g 4-cyanobenzaldehyde with 7.65 g benzyl carbamate and 13.5 mL tri- Ph phosphite in 20 mL glacial acetic acid gave 70% cyanophenylphosphonate II. Amidation of II with ammonia and ammonium chloride in MeOH gave amidophenyl derivative III as its HCl salt. III and related compds. were tested for inhibition of a variety of serine proteases.

AN 1999:582644 CAPLUS

DN 131:214554

TI Preparation of basic α -aminoalkylphosphonate derivatives as serine

protease inhibitors

IN Powers, James C.; Jackson, Delwin S.; Ni, Liming

PA Georgia Tech Research Corp., USA

SO U.S., 18 pp., Cont.-in-part of U.S. 5,696,419.

CODEN: USXKAM

DT Patent

LA English

PAN.CNT 2

PATENT NO. ----- KIND ----- DATE ----- APPLICATION NO. ----- DATE -----

10714255

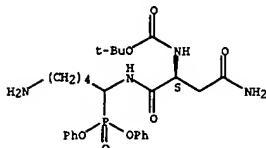
5/05/05

L12 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 PI US 5952307 A 19990914 US 1997-907840 19970814
 US 5686419 A 19971111 US 1994-184286 19940121
 PRAI US 1994-184286 A2 19940121

OS MARPAT 131:214554
 IT 242817-32-9P 242817-33-OP
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of basic α -aminoalkylphosphonate derivs. as serine protease inhibitors)

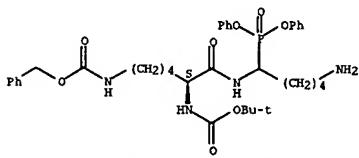
RN 242817-32-9 CAPLUS
 CN Carbamic acid, [(1S)-3-amino-1-[(5-amino-1-(diphenoxypyrophosphinyl)pentyl]amino]carbonyl]-3-oxopropyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 242817-33-0 CAPLUS
 CN Carbamic acid, [(1S)-1-[[[5-amino-1-(diphenoxypyrophosphinyl)pentyl]amino]carbonyl]-5-[(phenylmethoxy)carbonyl]amino]pentyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

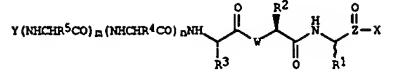
Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

GI



AB Compds. I [$Z = C$ or $P; X = CF_3, C_2F_5$, benzothiazole, CF_2CONHR_6 , $CONHR_6$ [$R_6 =$ alkyl, (n un)substituted Ph or cyclohexyl], etc.; $R_1 = H, Me, Et$; $R_2 = CH_2SO_2NH_2$, alkyl, arylalkyl, etc.]; $R_3 =$ alkyl, carboxyalkyl, adamantlyl; $R_4 =$ alkyl, arylalkyl; $R_5 = H, CH_2OH$; $Y = H, CH_2, CHMe$; $t-BuCH_2CH_2$, acyl, $n = 0, 1$] were prepared as inhibitor of the human cytomegalovirus (HCMV) protease. Thus, N1-(3,3,3-trifluoro-1-methyl-2-oxopropyl)-(2S)-2-[(1S)-2-methyl-1-[(1S)-2-methyl-1-[(methylcarboxamido)methyl]carboxamidopropyl]carboxamido]propylcarboxamido)butanediamide, prepared by the solid-phase method, showed $IC_{50} = 1.8 \pm 0.3 \mu M$ for inhibition of HCMV protease.

AN 1999-485077 CAPLUS

DW 129:122872

TI Peptidomimetic inhibitors of the human cytomegalovirus protease
 IN Bailey, Murray; Fazal, Gulrez; LaVallee, Pierre; Ogilvie, William; Poupart, Marc-Audre

PA Behringer Ingelheim (Canada) Ltd., Can.

SO PCI Int. Appl., 165 pp.

CODEN: PIXXD2

DT patent

LA English

FAN.CN1 1

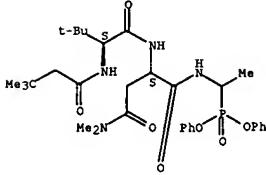
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 9829435 | A1 | 19980709 | WO 1997-CA1004 | 19971223 |
| W: CA, JP, MX, US
Rw: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 948523 | A1 | 19991013 | EP 1997-951048 | 19971223 |
| EP 948523 | B1 | 20040317 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI | | | | |
| JP 2001509418 | T2 | 20010626 | JP 1998-529511 | 19971223 |
| CA 2276109 | C | 20031118 | CA 1997-2276109 | 19971223 |
| CA 2276109 | AA | 19990709 | | |
| AT 261988 | E | 20040415 | AT 1997-951048 | 19971223 |
| US 6291640 | B1 | 20010918 | US 1998-171554 | 19981019 |
| PRAI US 1996-34041P | P | 19961227 | | |
| US 1997-52860P | P | 19970717 | | |
| US 1997-59806P | P | 19970923 | | |
| WO 1997-CA1004 | W | 19971223 | | |
| OS MARPAT 129:122872 | | | | |
| IT 198956-15-9P | | | | |

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L12 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (peptidomimetic inhibitors of the human cytomegalovirus protease)

RN 198956-15-9 CAPLUS
 CN L-Aspartamide, N-(3-dimethyl-1-oxobutyl)-3-methyl-L-valyl-N1-(1-(diphenoxypyrophosphinyl)ethyl)-N4,N4-dimethyl- (9CI) (CA INDEX NAME)

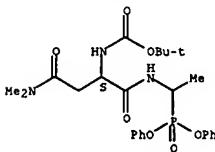
Absolute stereochemistry.



IT 198956-53-5P 198956-55-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (peptidomimetic inhibitors of the human cytomegalovirus protease)

RN 198956-53-5 CAPLUS
 CN Carbamic acid, [(1S)-3-(dimethylamino)-1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-oxopropyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

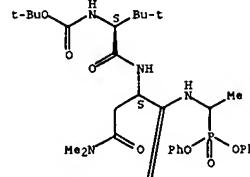
Absolute stereochemistry.



RN 198956-55-7 CAPLUS
 CN L-Aspartamide, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-N1-(1-(diphenoxypyrophosphinyl)ethyl)-N4,N4-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

10714255

5/05/05

L12 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AB One mechanism of killing by cytotoxic lymphocytes involves the exocytosis of specialized granules. The released granules contain perforin, which assembles into pores in the membranes of cells targeted for death. Serine proteases termed granzymes are present in the cytotoxic granules and include several chymases (with chymotrypsin-like specificity of cleavage). One chymase is selectively reactive with an inhibitor, biotinyl-Acs-Acs-Phe-Leu-Phe(Oph)2, that blocks perforin lysis. The authors report the purification and characterization of this chymase, lymphocyte chymase I, from rat natural killer cell (RNK)-16 granules. Lymphocyte chymase I is 30 kDa with a pH 7.5 to 9 optimum and primary substrate preference for tryptophan, a preference distinct from rat mast cell chymases. This chymase also reacts with other selective serine protease inhibitors that block perforin pore formation. It elutes by Cu²⁺-immobilized metal affinity chromatog. with other granzymes and has the N-terminal protein sequence conserved among granzymes. Chymase I reduces pore formation when preincubated with perforin at 37°. In contrast, addition of the chymase without preincubation had little effect on lysis. It should be noted that the perforin preparation contained sufficient residual chymase activity to support lysis. Thus, the reduction of lysis may represent an effect of excess proteolytic chymase I or a means to limit perforin lysis of bystander cells. In contrast, other chymases and granzyme K were without effect when added to perforin during similar preincubation. Identification of the natural substrate of chymase I will help resolve how it regulates perforin-mediated pore formation.

AN 1998:302495 CAPLUS
 DN 129:60594
 TI Purification and characterization of lymphocyte chymase I, a granzyme implicated in perforin-mediated lysis

AU Woodard, Susan L.; Frassetto, Stephanie A.; Winkler, Ulrike; Jackson, Delwin S.; Kan, Chih-Mini; Powers, James C.; Hudig, Dorothy
 CS Department of Microbiology, School of Medicine, University of Nevada, Reno, NV, 89557, USA
 SO Journal of Immunology (1998), 160(10), 4988-4993
 CODEN: JOMIA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journals

LA English

IT 199623-14-4 209338-74-0

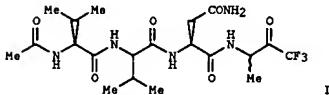
RL BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (Inhibition of lymphocyte chymase I by)

RN 195623-14-4 CAPLUS

CN L-Leucinamide, N-[6-[(6-[(3aS,4S,6aS)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl)amino]-1-oxohexyl]amino]-1-oxohexyl]-L-phenylalanyl-N-[1-(diphenoxyporphosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 GI



AB The development of peptidomimetic inhibitors of the human cytomegalovirus (HCMV) protease showing sub-micromolar potency in an enzymic assay is described. Selective substitution of the amino acid residues of these inhibitors led to the identification of tripeptide inhibitors showing improvements in inhibitor potency of 27-fold relative to inhibitor I based upon the natural tetrapeptide sequence. Small side chains at P1 were well tolerated by this enzyme, a fact consistent with previous observations. The S2 binding pocket of HCMV protease was very permissive, tolerating lipophilic and basic residues. The substitutions tried at P3 indicated that a small increase in inhibitor potency could be realized by the substitution of a tert-leucine residue for valine. Substitutions of the N-terminal capping group did not significantly affect inhibitor potency. Pentfluorooethyl and α-difluoro-β-keto amides, phosphonates and α-keto amides were all effective substitutions for the activated carbonyl component and gave inhibitors which were selective for HCMV protease. A slight increase in potency was observed by lengthening the P1' residue of the α-keto amide series of inhibitors. This position also tolerated a variety of groups making this a potential site for future modifications which could modulate the physicochem. properties of these mols.

AN 1997:72731 CAPLUS

DN 128:13422

TI Peptidomimetic Inhibitors of the Human Cytomegalovirus Protease
 AU Ogilvie, William; Bailey, Murray; Poupart, Marc-André; Abraham, Abraham; Bhawar, Amit; Bonneau, Pierre; Bordeleau, Josée; Bousquet, Yves; Chabot, Catherine; Duceppe, Jean-Simon; Fazal, Guilrez; Goulet, Sylvie; Grand-Maitre, Chantal; Guse, Ingrid; Holmes, Ted; Lavallée, Pierre; Leach, Michael; Malenfant, Eric; O'Meara, Jeff; Plante, Raymond; Plouffe, Celine; Poirier, Martin; Soucy, Francois; Youkam, Christiane; Deziel, Robert
 CS Bio-Mega Research Division, Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.
 SO Journal of Medicinal Chemistry (1997), 40(25), 4113-4135
 CODEN: JKMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT 198956-15-9P

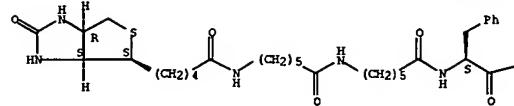
RL BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and structure-activity of peptidomimetic inhibitors of the human cytomegalovirus protease)

RN 198956-15-9 CAPLUS

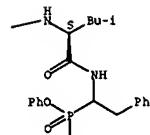
CN L-Aspartamide, N-(3,3-dimethyl-1-oxobutyl)-3-methyl-L-valyl-N1-(1-(diphenoxyporphosphinyl)ethyl)-N4,N4-dimethyl- (9CI) (CA INDEX NAME)

L12 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



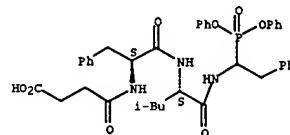
PAGE 1-B



RN 209335-74-0 CAPLUS

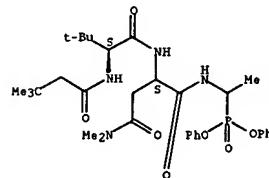
CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-L-phenylalanyl-N-[1-(diphenoxyporphosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 Absolute stereochemistry.



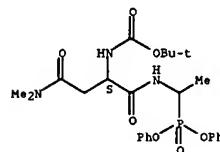
IT 198956-53-5P 198956-53-7P

RL RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and structure-activity of peptidomimetic inhibitors of the human cytomegalovirus protease)

RN 198956-53-5 CAPLUS

CN Carbamic acid, [(1S)-3-(dimethylamino)-1-[(1-(diphenoxyporphosphinyl)ethyl)amino]carbonyl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198956-53-7 CAPLUS

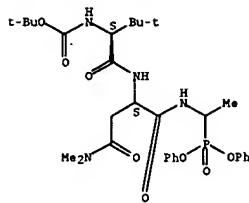
CN L-Aspartamide, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-N1-(1-(diphenoxyporphosphinyl)ethyl)-N4,N4-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10714255

5/05/05

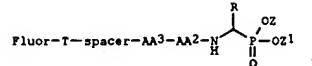
L12 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

GI



AB Fluorescent 1-peptidylaminoalkanephosphonate derivs. I [Fluor = 5- or 6-substituted fluorescein derivative, 5- or 6-substituted tetramethylrhodamine deriv, 5- or 6-substituted Texas Red derivative, other aromatic fluorescent group] with an emission maximum of 350-700 nm; T = NHCO, NHCS, CS, CO, SO2; spacer

= NH(CH2)5CO, NH(CH2)5CONH(CH2)5CO, other organic structure which is 3-24 Å long including at least group CH2CH2, CONH, NHCO, CH2CO, CH2NH, NHCH2, or CHSH in the backbone; AA3, AA2 = independently blocked or unblocked, L- or D-amino acid residue; R = side chain of blocked or unblocked amino acid, R-substituted Ph or benzyl, R-amino, guanidino, isothioureido, amino, B-substituted Ph or benzyl, B-amino, guanidino, isothioureido, amino; Z, Z1 = independently Ph substituted with 0-3 halo, Cl-6 alkyl, Cl-6 perfluoroalkyl, Cl-6 alkoxy, NO2, or CN groups], and their use in detecting and studying the distribution of serine proteases in cells and biol. systems are described. Thus, coupling of fluorescein isothiocyanate with Me 6-aminoacrylate, saponification of the Me ester, and peptide coupling

with tripeptide phosphonate analogs gave title compds. I [Fluor = 5-fluoresceinyl, T = CS, spacer NH(CH2)5CO]; AA3 = AA2 = Ala, R = Me, CH2CH2SH; AA3 = Phe, AA2 = Leu, R = CH2Ph] (II). II inhibited serine proteases with efficiencies equal to or greater than the corresponding N-tart-butoxycarbonyl (Boc) or N-benzyloxycarbonyl (Z) tripeptide phosphonates.

AN 1997701463 CAPLUS

DU 127:359112

II Preparation of fluorescent 1-peptidylaminoalkanephosphonate derivatives

IN Powers, James C.; Abuelyaman, Ahmed S.

PA Georgia Tech Research Corp., USA

SO U.S., 14 pp.

CODEN: USXKAM

DT Patent

LA English

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI US 5681821 | A | 19971028 | US 1994-324809 | 19941018 |
| US 5916877 | A | 19990629 | US 1997-911380 | 19970814 |
| PRAI US 1994-324809 | AZ | 19941018 | | |
| OS MARPAT 127:59112 | | | | |
| IT 197857-46-EP 197984-51-3P 198629-89-9P | | | | |

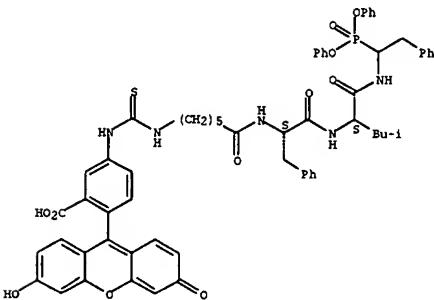
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L12 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (prep. of fluorescent peptidylaminoalkanephosphonate derivs. for detecting serine proteases in biol. media)

RN 197857-46-8 CAPLUS

CN L-Leucinamide, N-(6-[[[3-carboxy-4-(6-hydroxy-3-oxo-3H-kanthren-9-yl)phenyl]amino]thiomethyl]amino)-1-oxohexyl)-L-phenylalananyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

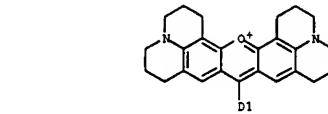
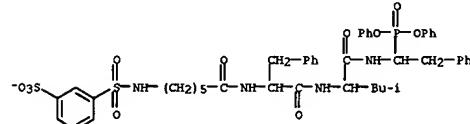
Absolute stereochemistry.



RN 197984-51-3 CAPLUS

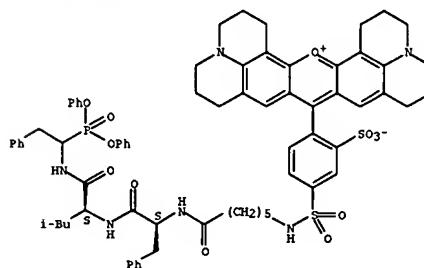
CN L-Leucinamide, N-[6-[[[2(or 4)-(2,3,6,7,12,13,16,17-octahydro-1H,5H,11H,15H-xantheno[2,3,4-i:j:5,6,7-i'j']diquinolinizin-18-iium-9-y1)-5-sulfophenyl]sulfonyl]amino]-1-oxohexyl]-L-phenylalananyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]-, inner salt (9CI) (CA INDEX NAME)

L12 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 198629-89-9 CAPLUS
CN L-Leucinamide, N-[6-[[[4-(2,3,6,7,12,13,16,17-octahydro-1H,5H,11H,15H-xantheno[2,3,4-i:j:5,6,7-i'j']diquinolinizin-18-iium-9-y1)-3-sulfophenyl]sulfonyl]amino]-1-oxohexyl]-L-phenylalananyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 157197-34-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluorescent peptidylaminoalkanephosphonate derivs. for detecting serine proteases in biol. media)

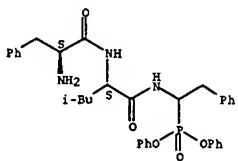
RN 157197-34-7 CAPLUS

CN L-Leucinamide, L-phenylalananyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

10714255

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L12 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Absolute stereochemistry.



● HCl

L12 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AB Di-Ph 1-(N-peptidylamino)alkanephosphonate esters are highly reactive, specific, and aqueously stable irreversibly inhibitors which can be used to probe the functions of many serine proteases, including the lymphocyte granzymes. We synthesized 10 peptide phosphonates with Ala, Met, Phe, or Val at the P1 amino acid residues, including two biotinylated derivs. for future functional and biochemical characterization of granzymes. The reactivity of the inhibitors was characterized with human leukocyte elastase (HLE), porcine pancreatic elastase (PPE), bovine chymotrypsin, and the granzymes of natural killer (NK) cells, which include a number of proteolytic activities (Asp-ase, Met-ase, etc.) that cleave peptide substrates with these residues in the P1 position. The reactivity and specificity of the phosphonates depended on the length and sequence of the peptidyl moiety and on the leaving group. Z-Ala-Ala-Ala-P(OBu)2 was a good inhibitor of HLE and PPE (kobsd/[I] = 30 and 30 M-1-s-1, resp.) and had little reactivity with chymotrypsin. Z-Phe-Pro-Phe-P(OBu)2 was a good inhibitor of chymotrypsin (kobsd/[I] = 17,000 M-1-s-1) and had little reactivity with the elastases. The leaving group of Z-Met-P(OBu-4-Cl)2 made it a more effective chymotrypsin inhibitor than Z-Met-P(OBu)2 (kobsd/[I] values of 142 and 30 M-1-s-1, resp.). With granzymes, the compds. reacted with a fraction of the Met-ase, chymase, and Ser-ase activities and lacked reactivity with Asp-ase and tryptase. Z-Met-P(OBu-4-Cl)2 was an excellent inhibitor of Met-ase I. Bi-Aca-Aca-Phe-Leu-Phe(P(OBu)2 appears to react specifically with one chymase while leaving other chymases untouched. Perforin-dependent lysis mediated by cytotoxic lymphocyte granules was inactivated by Z-Ala-Ala-Ala-P(OBu)2, Z-Met-P(OBu-4-Cl)2, Z-Leu-Phe(P(OBu)2, and Bi-Aca-Aca-Phe-Leu-Phe(P(OBu)2. The biochemical properties and biological efficacy of these inhibitors make them suitable for cellular and physiological studies of granzyme function.

AN 1997545924 CAPLUS

DN 127-244673

TI Synthesis and kinetic studies of diphenyl 1-(N-peptidylamino)alkanephosphonate esters and their biotinylated derivatives as inhibitors of serine proteases and probes for lymphocyte granzymes

AU Abuselyaman, Ahmed S.; Jackson, Delwin S.; Hudig, Dorothy; Woodard, Susan L.; Powers, James C.

CS Georgia Institute of Technology, The School of Chemistry and Biochemistry, Atlanta, GA, 30332-0400, USA

SO Archives of Biochemistry and Biophysics (1997), 344(2), 271-280

CODEN: ABBIA4; ISSN: 0003-9861

PB Academic

DR Journal

LA English

IT 157197-29-0P 195623-13-3P 195623-14-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

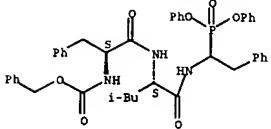
(synthesis and kinetic studies of di-Ph 1-(N-peptidylamino)alkanephosphonate esters and biotinylated derivs. as inhibitors of serine proteases and probes for lymphocyte granzymes)

RN 157197-29-0 CAPLUS

CN L-Leucinamide, N-[{(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl] - (9CI) (CA INDEX NAME)

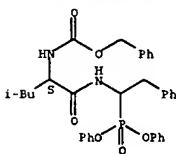
Absolute stereochemistry.

L12 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 195623-13-3 CAPLUS
CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)-2-phenylethyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

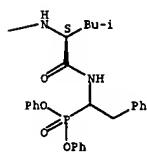


RN 195623-14-4 CAPLUS
CN L-Leucinamide, N-[6-[(6-[(3aS,4S,6aS)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl)amino]-1-oxohexyl]amino]-1-oxohexyl]-L-phenylalanyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-B



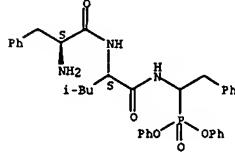
IT 157197-34-7 195623-18-8

RL: RCT (Reactant or reagent); RACT (Reactant or reagent)
(synthesis and kinetic studies of di-Ph 1-(N-peptidylamino)alkanephosphonate esters and biotinylated derivs. as inhibitors of serine proteases and probes for lymphocyte granzymes)

RN 157197-34-7 CAPLUS

CN L-Leucinamide, L-phenylalanyl-N-[1-(diphenoxypyrophosphinyl)-2-phenylethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

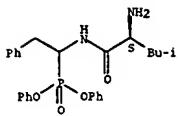
RN 195623-18-8 CAPLUS
CN Phosphoric acid, [1-[(2-amino-4-methyl-1-oxopentyl)amino]-2-phenylethyl]-, diphenyl ester, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L12 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

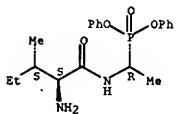
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AB A number of dipeptide di-Ph phosphonate esters were studied as inhibitors of dipeptidyl peptidase IV, focusing on the role of the P2 residue in the inactivation process. The active compds. were slow irreversible inhibitors of the catalytic activity of the enzyme. With proline (or alanine) in the P1 position, the rate consts. of inactivation correlated with the acylation rate consts., reported for homologous dipeptide derived substrates. The kinetic data indicate that the mechanism of inhibition consists of the formation of a fairly weak initial complex, followed by a slow irreversible inactivation step. This indicates that, as in the case of trypsin-like proteinases, dipeptide di-Ph phosphonate esters form a covalent adduct with the catalytic site of DPP IV, even though this enzyme belongs to a completely distinct class of serine peptidases. Enantioselectivity and secondary specificity further support the evidence that di-Ph phosphonate esters are mechanism-based inhibitors. The dipeptide di-Ph phosphonate esters had a half-life of 3-10 h at 37° in Tris buffer. The inhibitors were degraded in human plasma, depending on the type of amino-terminal amino acid. The compound with proline in the P2 position was the most resistant to degradation in plasma. Due to their stability and the irreversible nature of the inhibition, the di-Ph phosphonate esters promise to be useful tools in the continuing investigation of the physiol. function of dipeptidyl peptidase IV.

AN 1996296800 CAPLUS
DN 125;52112
TI Dipeptide-derived diphenyl phosphonate esters: mechanism-based inhibitors of dipeptidyl peptidase IV
AU Lambre, Anna-Marie; Borloo, Marianne; De Meester, Ingrid; Belyaev, Alexander; Augustyns, Koen; Hendriks, Dirk; Scharpe, Simon; Haemers, Achiel
CS Laboratories of Medical Biochemistry and Pharmaceutical Chemistry, Department of Pharmaceutical Sciences, University of Antwerp (U.I.A.), Wilrijk, B-2610, Belg.
SO Biochimica et Biophysica Acta (1996), 1290(1), 76-82
CODEN: BBACAO ISSN: 0006-3002
PB Elsevier
DT Journal
LA English
IT 177599-07-4 178150-13-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(dipeptide-derived di-Ph phosphonate esters as mechanism-based inhibitors of dipeptidyl peptidase IV)
RN 177599-07-4 CAPLUS
CN Phosphonic acid, [(1S)-1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]ethyl]-, diphenyl ester, [2S-1(S),2R*,3R*]- (9CI) (CA INDEX NAME)

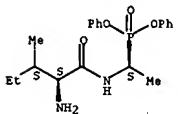
Absolute stereochemistry.

L12 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 178150-13-5 CAPLUS
CN Phosphonic acid, [(1S)-1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]ethyl]-, diphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

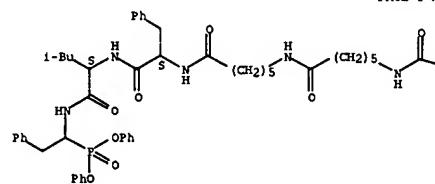


L12 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AB An irreversible serine protease inhibitor, biotinyl-Aca-Aca-Phe-Leu-PheP(OPh)2, was shown to selectively inhibit a chymotrypsin-like (chymase) serine protease activity of rat RNK-16 granule exts. Under the same conditions, only one 30-kDa (reduced) band was detected on protein blots. Furthermore, only 1 of 3 chymase peaks separated by hydrophobic interaction chromatog. was inhibited. When this granzyme was inhibited, granule-mediated lysis of erythrocytes was diminished. NK cell killing was completely blocked when biotinyl-Aca-Aca-Phe-Leu-PheP(OPh)2 was added to cytotoxicity assays at 200 μM with rat splenocytes as effectors. By confocal fluorescence microscopy, it was shown that this inactivated the chymase activity and reduced lysis found in their dense organelles. Together these data indicate that biotinyl-Aca-Aca-Phe-Leu-PheP(OPh)2 inhibits a granule chymase that is essential to cytolytic activity of NK cells.

AN 1995225014 CAPLUS
DN 122:312860
TI Chymase-directed serine protease inhibitor that reacts with a single 30-kDa granzyme and blocks NK-mediated cytotoxicity
AU Woodard, Susan L.; Jackson, Delwin S.; Abuelyaman, Ahmed S.; Powers, James C.; Winkler, Ulrike; Hudig, Dorothy
CS Dept. Microbiology, Univ. Nevada, Reno, NV, 89557, USA
SO Journal of Immunology (1994), 153(11), 5016-25
CODEN: JOMHA3 ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
IT 163518-06-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(chymase-directed serine protease inhibitor that reacts with single 30-kDa granzyme and blocks NK-mediated cytotoxicity)
RN 163518-06-7 CAPLUS
CN L-leucinamide, N-[6-[(6-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]-1-oxohexyl)amino]-1-oxohexyl]-L-phenylalanyl-N-[1-(diphenoxophosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

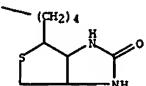


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L12 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-B



L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Three fluorescein- and one Texas Red-labeled derivs. of [1-(N-dipeptidylamino)alkyl]phosphonate di-Ph esters were synthesized and evaluated as inhibitors of serine proteases. The two fluorophores, FITC and TRX, were attached to the peptide phosphonates via an ϵ -aminocaproic unit that acts as a spacer group and facilitates the binding of the phosphonate inhibitor to the targeted enzymes. These derivs. are potent and specific inhibitors of chymotrypsin, porcine pancreatic elastase (PPE), and human leukocyte elastase (HLE). FITC-Aca-Phe-Leu-PheF(OPh)2 (3), inhibited chymotrypsin very potently ($K_{iD}/[I] = 9500 \text{ M}^{-1} \text{ s}^{-1}$) and 600-fold better than it did PPE ($K_{iD}/[I] = 16 \text{ M}^{-1} \text{ s}^{-1}$). FITC-Aca-Ala-Ala-MetF(OPh)2 (1) was a more effective inhibitor of chymotrypsin ($K_{iD}/[I] = 190 \text{ M}^{-1} \text{ s}^{-1}$) than PPE and HLE ($K_{iD}/[I] = 13$ and $22 \text{ M}^{-1} \text{ s}^{-1}$, resp.). Only HLE and PPE were inhibited by FITC-Aca-Ala-Ala-MetF(OPh)2 (2) ($K_{iD}/[I] = 41$ and $22 \text{ M}^{-1} \text{ s}^{-1}$, resp.). The specificity of these inhibitors toward the targeted serine proteases depended on the sequence of the tripeptide portion and was not affected by the presence of the fluorescent label. Trypsin, for instance, was not inhibited by any of these compds. In some cases, the inhibitory potency was increased by the fluorescent label. For example, chymotrypsin was inhibited by the fluorescein compds., FITC-Aca-Ala-Ala-MetF(OPh)2 (1) and FITC-Aca-Phe-Leu-PheF(OPh)2 (3), more potently than by the nonfluorescent compds., Boc-Ala-Ala-MetF(OPh)2 (5) and 2-Fhe-Leu-PheF(OPh)2 (7). Initial expts. with cytotoxic lymphocytes indicate that FITC-Aca-Ala-Ala-MetF(OPh)2 labels discrete granule-like regions where the serine proteases of the NK cell line, RAN-16, are stored.

AN 1995:21000 CAPLUS

DN 122:49805

TI Fluorescent Derivatives of Diphenyl [1-(N-Peptidylamino)alkyl]phosphonate Esters: Synthesis and Use in the Inhibition and Cellular Localization of Serine Proteases

AU Abubakar, Ahmad S.; Hudig, Dorothy; Woodard, Susan L.; Powers, James C.
 CS School of Chemistry and Biochemistry, Georgia Institute of Technology,
 Atlanta, GA, 30332-0400, USA

SO Bioconjugate Chemistry (1994), 5(5), 400-5

CODEN: BCCHES; ISSN: 1043-1802

DT Journal

LA English

IT 157197-36-9P 160041-08-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and serine proteinases inhibition by)

RN 157197-36-9 CAPLUS

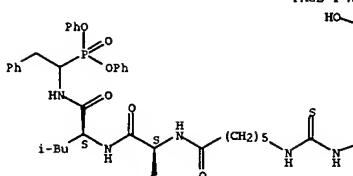
CN L-Leucinamide, N-[6-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thiomethyl]amino]-1-oxohexyl-L-phenylalanyl-N-[1-(diphenoxyporphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

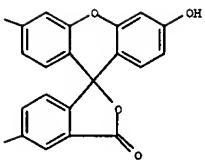
L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A

HO



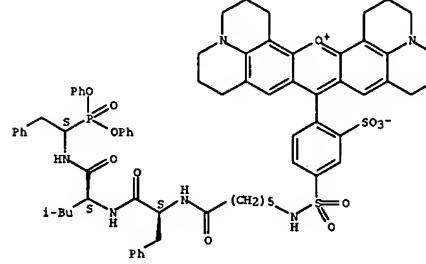
PAGE 1-B



RN 160041-08-7 CAPLUS
 CN L-Leucinamide, N-[6-[[[(2,3,6,7,12,13,16,17-octahydro-1H,5H,11H,15H-xantheno[2,3,4-i;j,5,6,7-1'j]diquinolizin-18-ium-9-y]-3-sulfophenyl)sulfonyl]amino]-1-oxohexyl]-L-phenylalanyl-N-[1-(diphenoxyporphinyl)-2-phenylethyl]-, inner salt, (S)- (9CI) (CA INDEX NAME)

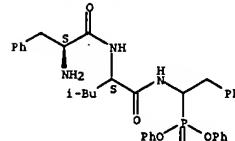
Absolute stereochemistry.

L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT 157197-34-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with fluorescent aminocaproic acid derivative)
 RN 157197-34-7 CAPLUS
 CN L-Leucinamide, L-phenylalanyl-N-[1-(diphenoxyporphinyl)-2-phenylethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 157197-29-0
 RL: BIOL (Biological study)
 (serine proteinases inhibition by, fluorescent analog in relation to)
 RN 157197-29-0 CAPLUS
 CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[1-(diphenoxyporphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

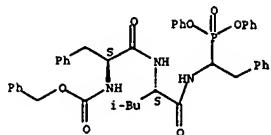
Absolute stereochemistry.

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L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



L12 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

GI



AB Derivs. of α -amino acids with 2 stereogenic centers (cf. L-threonine) and of di-, tri-, and tetrapeptides are electrolyzed in MeOH or AcOH, with formation of N-acyl-N,O-acetals, in an anodic oxidative substitution of the COOH by an OR group. Thus, the electrochemical decarboxylation of protected dipeptides Z-Ala-Ala-OH (Z = PhCH₂O₂C) in MeOH give 2-Ala-NHCH(OMe)Me. With unprotected dipeptides, e.g. N-Ala-Ala-OH, the electrochem. decarboxylation may give imidazolidinones, e.g. I, in NH₄OAc/H₂O. The electrolyses are carried out in simple flasks with cooling jackets (undivided cell), using constant current conditions and anodes of Pt or glassy C. The electrolyte is generated in situ by adding 10–20 mol-% of a tertiary amine. Mild acidic hydrolysis of electrolysis products thus obtained may lead to amino acid amides or peptide amides with 1 amino acid less than the starting material. The N,O-acetals from L-threonine and the oligopeptides also react with organometallic nucleophiles, such as Grignard compds., with formation of products in which the original COOH group has been replaced by alkyl or allyl (sometimes even with moderate stereoselectivity). By treatment of the peptides-derived (open-chain) N,O-acetals with trialkyl or triaryl Phosphites/TiCl₄, the RO group is replaced by a phosphodiester group in a (non-diastereoselective) Michaelis-Arbuzov-type reaction. Thus, the 2-step sequence of electrolysis and phosphorylation converts an oligopeptide derivative to an analog with a phosphonic acid end group. The diastereoisomeric N-protected di-L-He and di-D-Asp dipeptidophosphonates could be separated by preparative HPLC.

AN 1990:179809 CAPLUS

DN 112:179809

TI Electrochemical decarboxylation of L-threonine and oligopeptide derivatives with formation of N-acyl-N,O-acetals; preparation of oligopeptides with amide or phosphonate C-terminus

AU Seebach, Dieter; Charczuk, Roland; Gerber, Christian; Renaud, Philippe; Berner, Heinz; Schneider, Helmut

CS Helveticia Chimica Acta (1989), 72(3), 401-25

SO CODEN: HCACAV; ISSN: 0018-019X

DT Journal

LA German

OS CASREACT 112:179809

IT 126306-94-3P 126306-95-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

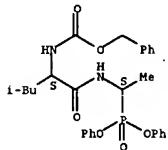
(preparation and hydrolysis of)

RN 126306-94-3 CAPLUS

CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-

L12 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

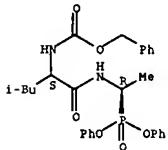
Absolute stereochemistry.



RN 126306-95-4 CAPLUS

CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 82818-40-4 CAPLUS

CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

L12 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AB In the synthesis of phosphopeptides H-X-NHCHR_P(O)2 (I; X = Ala, Leu, R = Me; X = Ala, Val, Leu, Pro, R = CHMe₂; X = Val, Leu, Pro, R = CH₂CHMe₂) from the corresponding Z-X-OH (Z = PhCH₂O₂C) and H₂NCHR_P(O)(OPh)₂, the removal of the Ph group from the resulting Z-X-NHCHR_P(O)(OPh)₂ was achieved by a transesterification with MeOH/KF/crown ether to give Z-X-NHCHR_P(O)(OMe)2 which was then deblocked by HBr/HOAc to give the appropriate I.

AN 1982:510377 CAPLUS

DN 97:110377

TI Transesterification of diphenyl phosphonates using the potassium fluoride/crown ether/alcohol system. Part 2. The use of diphenyl 1-aminoalkanephosphonates in phosphopeptide synthesis

AU Lejczak, Barbara; Kafarski, Pawel; Szewczyk, Jerzy

CS Inst. Org. Phys. Chem., Tech. Univ. Wroclaw, Wroclaw, 50-370, Pol.

SO Synthesis (1982), (5), 412-14

CODEN: SYNTBF; ISSN: 0039-7881

DT Journal

LA English

OS 82818-40-4P 82818-43-7P 82818-46-0P

IT 82818-40-4P 82818-43-7P 82818-46-0P

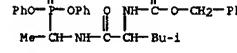
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and transesterification of, with methanol in presence of

potassium fluoride and crown ether)

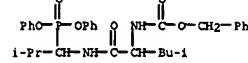
RN 82818-40-4 CAPLUS

CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)ethyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



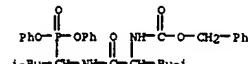
RN 82818-43-7 CAPLUS

CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)-2-methylpropyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 82818-46-0 CAPLUS

CN Carbamic acid, [1-[(1-(diphenoxypyrophosphinyl)-3-methylbutyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



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L12 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

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ENTRY | TOTAL
SESSION |
| FULL ESTIMATED COST | 88.93 | 737.04 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE
ENTRY | TOTAL
SESSION |
| CA SUBSCRIBER PRICE | -12.41 | -12.41 |

STN INTERNATIONAL LOGOFF AT 14:41:08 ON 05 MAY 2005

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